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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/446,089	12/17/1999	Keiko Sakakibara	001560-377	1763

7590 01/14/2004

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/446,089	SAKAKIBARA ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003 and 04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,18 and 22-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *31,32 and 36* is/are allowed.

6)☒ Claim(s) *1,5-9,18,22-30,33-35 and 37-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 5/6/03 has been entered.

2. Claims 1, 5, 18, and 22 have been amended and claims 2-4 and 19-21, have been canceled, and claims 27-43 have been added. Claims 1, 5-9 and 18, 22-43 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s):

The sequence disclosed in the specification at page 22 as SEQ ID NO: 6 differs from the sequence listed in the sequence listing as SEQ ID NO: 6. Namely, the sequence in the

specification has an isoleucine residue at the third position of the amino acid sequence, while the sequence in the sequence listing has an aspartic acid residue at the third position of the amino acid.

Proper correction is required.

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit, as needed, a new CRF and paper copy of the Sequence Listing containing these sequences, in addition to the previously listed sequences, an amendment directing the entry of the Sequence Listing into the specification, an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same.

Specification

The amendment filed 6/1/01 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: In the newly filed sequence listing, the recitation of SEQ ID NO: 6 does not appear to be supported in the specification. The sequence disclosed as SEQ ID NO: 6 in the newly filed sequence listing is not identical to the sequence disclosed as SEQ ID NO: 6 in the specification and sequence listing as originally filed because the SEQ ID NO: 6 in the newly filed sequence listing has an aspartic acid residue at the third position of the amino acid sequence, while the sequence in the originally filed specification and sequence listing has an isoleucine residue at the third position of the amino acid.

3. Applicant is required to cancel the new matter in the reply to this Office Action. Such a cancellation must in compliance with the sequence rules (i.e. a new paper copy of the sequence listing and CRF must be filed).

Claim Rejections - 35 USC § 112

4. Claims 1, 5-9, 18, 22, 23, 24, 25, 26, 38, 39, 40, 41, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In claims 1, 5-9, 18, 22, 23, 24, 25, 26, 38, 39, 40, 41, 42, and 43, the new limitation of "wherein said gene is obtained from *Scrophulariales*" in claims 1 and 18 appears to represent new matter. No specific basis for this limitation was identified in the specification, nor did a review of the specification by the examiner find any basis for the limitation. Applicant's remarks on page 7 state that "Antirrhinum majus is a species of the family *Scrophulariales*," but applicant does not point to any portion of the specification or claims as originally filed which contemplates the genus of isolated genes or nucleic acids encoding a protein having activity to synthesize aurones using chalcones as substrates, wherein the gene or nucleic acid is obtained from *Scrophulariales*. Since no basis has been identified, the claims are rejected as incorporating new matter. The remaining rejected claims all depend from claim 1 or claim 18 and are rejected as incorporating new matter for the same reason.

In claims 37, 39, 41, and 43 the recitation of SEQ ID NO: 6 as it pertains to the sequence present in the sequence listing is new matter because this sequence is not present in the specification or claims as originally filed (see new matter objection and sequence rules objection herein).

5. Claims 37, 39, 41, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 is indefinite over the recitation "includes at least one amino acid sequence of SEQ ID Nos: 3, 4, 5, 6, and 7" because it is not clear if this language means that the claimed nucleic acid encodes a protein which comprises on of the recited sequences or if the language means that the claimed nucleic acid encodes a protein which comprises a portion ("at least one amino acid of") one of the recited sequences.

All of the rejected claims are indefinite over the recitation of SEQ ID NO: 6, because it is not clear which version of SEQ ID NO: 6 is being referred to. The specification and sequence listing both disclose a SEQ ID NO: 6, but these two molecules are not the same, as noted in the sequence rules compliance notice within this office action. Thus, it is not clear which sequence applicant is referring to when applicant refers to "SEQ ID NO: 6."

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 5-9, 18, 21-26, 27-30, 33, 34, 35, and 37-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a

protein having activity to synthesize aureusidin by using chalcones as substrates, wherein the nucleic acid comprises a sequence encoding SEQ ID NO: 2, does not reasonably provide enablement for any other nucleic acids encoding such proteins, or for nucleic acids encoding proteins that have the ability to synthesize any other aurones. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Instant claim 1 encompasses an isolated gene which encodes a protein having activity to synthesize aurones using chalcones as substrates, wherein said gene is obtained from *Scrophulariales*. Claims 5 each depends from claim 1 and recites that the claimed gene encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence described in SEQ ID NO: 2 and encodes a protein having activity to synthesize aurones using chalcones as substrates. Claims 6-9 recite vectors and host cells. Thus, the scope of claim 1 and the claims which depend from claim 1 encompass nucleic acids from any plant within the family Scrophulariales (there are 95 genera within this family most having multiple species). Furthermore, claim 1 recites an isolated "gene" which encompasses genomic DNAs that include untranslated regions such as promoters and introns and 3' regulatory regions.

Claim 18 is drawn to an isolated nucleic acid encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates, wherein said gene is obtained from *Scrophulariales*. Claim 22 each depends from claim 18 recites that the claimed gene encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence described in SEQ ID NO: 2 and encodes a protein having activity to synthesize aurones using chalcones as substrates. Claims 23-26 recite vectors and host cells. Claims 38, 40, and 42

depend from claim 22 and recite that the encoded amino acid sequence have 70%, 80%, and 90% homology to SEQ ID NO: 2, respectively. Claims 39, 41, and 43 depend from claims 38, 40, and 42 and recite that the encoded amino acid sequence include at least one amino acid sequence selected from the group consisting of SEQ ID NO: 3, 4, 5, 6, and 7. Thus, the scope of claim 1 and the claims which depend from claim 1 encompass nucleic acids from any plant within the family Scrophulariales (there are 95 genera within this family most having multiple species). Furthermore, claims 39, 41, and 43 expressly encompass nucleic acids which encode SEQ ID NO: 6 and SEQ ID NO: 7, both of which are amino acid fragments which do not share 100% identity with portions of SEQ ID NO: 2. Namely, SEQ ID NO: 6 in the sequence listing differs from a fragment of SEQ ID NO: 2 in that it has one less isoleucine residue than the corresponding portion of SEQ ID NO: 2, and SEQ ID NO: 7 differs from SEQ ID NO: 2 in that it has a glycine at position 121 while SEQ ID NO: 2 has a glutamic acid at the corresponding position.

Claim 27 is drawn to an isolated nucleic acid obtained from Antirrhinum majus encoding a protein having an activity to synthesize aurones using chalcones as substrates. Claims 28-30 depend from claim 27 and recite vectors and host cells. Claim 37 recites that the encoded protein encodes at least one amino acid sequence of SEQ ID NO: 3, 4, 5, 6, and 7. Furthermore, 37 expressly encompasses nucleic acids which encode SEQ ID NO: 6 and SEQ ID NO: 7, both of which are amino acid fragments which do not share 100% identity with portions of SEQ ID NO: 2. Namely, SEQ ID NO: 6 in the sequence listing differs from a fragment of SEQ ID NO: 2 in that it has one less isoleucine residue than the corresponding portion of SEQ ID NO: 2, and SEQ

ID NO: 7 differs from SEQ ID NO: 2 in that it has a glycine at position 121 while SEQ ID NO: 2 has a glutamic acid at the corresponding position.

Claim 35 is drawn to an isolated gene encoding a protein having activity to synthesize aurones using chalcones as substrates, wherein said protein has the amino acid sequence of SEQ ID NO: 2. Claim 35 recites an isolated "gene" which encompasses genomic DNAs that include untranslated regions such as promoters and introns and 3' regulatory regions.

Furthermore, it is noted that claims 7, 8, 24, 25, 33, and 34 recite include the recitation of a "host cell" which encompasses whole organisms such as transgenic animals for which no disclosure or support is provided (see specification page 9). To make and use such animals would require undue experimentation as it is entirely unknown how the expression of the instantly disclosed nucleic acids would effect such animals. The amendment of these claims to clarify that the "host cells" are isolated would overcome this concern.

The specification teaches a single cDNA molecule (SEQ ID NO: 1) which encodes the polypeptide SEQ ID NO: 2. The working examples demonstrate that the polypeptide encoded by SEQ ID NO: 1 has the ability to synthesize aureusidin by using chalcones as substrates (Examples 3 and 6). The specification further teaches that the enzyme tyrosinase form the organisms Neurospora also has the ability to synthesize aureusidin by using chalcones as substrates (Example 18). The nucleic acid encoding the Neurospora tyrosinase was known in the prior art at the time the invention was made (see Kupper *et al.* and 102(b) rejections below), but does not fall within the scope of the instantly rejected claims because it is not isolated from one of the recited organisms. The specification also teaches that instant SEQ ID NO: 2 has a copper binding region that is typical of the active center of polyphenol oxidases (Example 10).

The specification at page 5 generically discusses that enzymes have regions that are essential and non-essential for enzyme activity, but the specification does not provide examples of any of these regions for instant SEQ ID NO: 2. Further, the specification provides fragments of SEQ ID NO: 2 that were sequenced prior to the isolation of the full length SEQ ID NO: 1 from which SEQ ID NO: 2 was deduced. These fragments are SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, and SEQ ID NO: 6 as disclosed in the specification (as opposed to within the sequence listing). The specification within example 9 teaches the isolation of a nucleic acid encoding a partial enzyme, that is SEQ ID NO: 7 via subtractive hybridization. The specification does not provide a full length cDNA that encodes SEQ ID NO: 7. The specification does not demonstrate that any of these fragments is sufficient to confer on an enzyme the ability to synthesize aureusidin using chalcones as substrates.

The specification and the prior art are silent as to any other polypeptides that have the ability to synthesize aureusidin by using chalcones as substrates, or any polypeptides that have the ability to synthesize any other aurones (other than aureusidin) from chalcones. The specification does not provide any guidance as to what portions or fragments of instant SEQ ID NO: 2 are necessary to retain this activity. Neither the specification nor the prior art establish any relationship between all polypehnol oxidases and the activity that is attributed to instant SEQ ID NO: 2 and the Neurospora tyrosinase.

There are many polyphenol oxidase molecules (and nucleic acids encoding them) known in the prior art (see, for example, Hunt *et al.*, cited in paper number 30, Boss *et al.* and Robinson *et al.*, discussed below). However, neither the specification nor the prior art provide any guidance that would lead any person skilled in the art to select of all of the possibilities which

nucleic acids already discovered, or yet to be discovered, would possess the ability to synthesize aureusidin by using chalcones as substrates, or the ability to synthesize any other aurone using chalcones as substrates. Particularly, the neither the specification nor the prior art provide any guidance as to which nucleic acids encoding polyphenol oxidase enzymes encode those that use chalcones as substrates. In fact the only common structural feature that the specification has suggested that instant SEQ ID NO: 2 has with polyphenol oxidases is the fact that it has a copper binding region.

While the level of skill in the relevant art is quite high (PhD in biochemistry), the level of unpredictability is higher with regard to the ability to change an amino acids in a particular sequence while still retaining the functionality of the enzyme. The specification provides absolutely no guidance as to which or how many of the amino acids of instant SEQ ID NO: 2 can be changed yet still result in a polypeptide which retains the ability to synthesize aureusidin by using chalcones as substrates, particularly by preferentially using chalcones as substrates. Further, the specification gives no guidance as to the structure or identity of nucleic acids encoding any other sequence that has the ability to synthesize aurones other than aureusidin.

The identification of other nucleic acids that fall within the scope of the instantly claimed invention would require the screening of every possible enzyme isolated from the recited organisms to determine if they have the recited functionality. Such a search would be complicated by the fact that the skilled artisan would have no guidance as to which enzymes which are known or unknown would fall within the scope of the claimed invention.

Because of the breadth of the claims, the provision of only two sequences with the ability to synthesize aureusidin by using chalcones as substrates, the lack of any showing that other

aurones could be synthesized, the fact that full length genes are not provided which encode polypeptides shown to have the ability to synthesize aureusidin by using chalcones as substrates, the lack of direction in the specification of the identity and structure of other such enzymes, and the large quantity of experimentation necessary to identify other members of the claimed group, it is concluded that undue experimentation would be necessary to practice the claimed invention commensurate in scope with the instantly rejected claims.

8. Claims 1, 5-9, 18, 21-26, 27-30, 35, and 37-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Instant claim 1 encompasses an isolated gene which encodes a protein having activity to synthesize aurones using chalcones as substrates, wherein said gene is obtained from *Scrophulariales*. Claims 5 each depends from claim 1 and recites that the claimed gene encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence described in SEQ ID NO: 2 and encodes a protein having activity to synthesize aurones using chalcones as substrates. Claims 6-9 recite vectors and host cells. Thus, the scope of claim 1 and the claims which depend from claim 1 encompass nucleic acids from any plant within the family Scrophulariales (there are 95 genera within this family most having multiple species). Furthermore, claim 1 recites an isolated "gene" which encompasses genomic DNAs that include untranslated regions such as promoters and introns and 3' regulatory regions.

Claim 18 is drawn to an isolated nucleic acid encoding a protein having activity to synthesize aurones by preferentially using chalcones as substrates, wherein said gene is obtained from *Scrophulariales*. Claim 22 each depends from claim 18 recites that the claimed gene encodes an amino acid sequence having a homology of at least 55% relative to the amino acid sequence described in SEQ ID NO: 2 and encodes a protein having activity to synthesize aurones using chalcones as substrates. Claims 23-26 recite vectors and host cells. Claims 38, 40, and 42 depend from claim 22 and recite that the encoded amino acid sequence have 70%, 80%, and 90% homology to SEQ ID NO: 2, respectively. Claims 39, 41, and 43 depend from claims 38, 40, and 42 and recite that the encoded amino acid sequence include at least one amino acid sequence selected from the group consisting of SEQ ID NO: 3, 4, 5, 6, and 7. Thus, the scope of claim 1 and the claims which depend from claim 1 encompass nucleic acids from any plant within the family Scrophulariales (there are 95 genera within this family most having multiple species). Furthermore, claims 39, 41, and 43 expressly encompass nucleic acids which encode SEQ ID NO: 6 and SEQ ID NO: 7, both of which are amino acid fragments which do not share 100% identity with portions of SEQ ID NO: 2. Namely, SEQ ID NO: 6 in the sequence listing differs from a fragment of SEQ ID NO: 2 in that it has one less isoleucine residue than the corresponding portion of SEQ ID NO: 2, and SEQ ID NO: 7 differs from SEQ ID NO: 2 in that it has a glycine at position 121 while SEQ ID NO: 2 has a glutamic acid at the corresponding position.

Claim 27 is drawn to an isolated nucleic acid obtained from Antirrhinum majus encoding a protein having an activity to synthesize aurones using chalcones as substrates. Claims 28-30 depend from claim 27 and recite vectors and host cells. Claim 37 recites that the encoded protein

encodes at least one amino acid sequence of SEQ ID NO: 3, 4, 5, 6, and 7. Furthermore, 37 expressly encompasses nucleic acids which encode SEQ ID NO: 6 and SEQ ID NO: 7, both of which are amino acid fragments which do not share 100% identity with portions of SEQ ID NO: 2. Namely, SEQ ID NO: 6 in the sequence listing differs from a fragment of SEQ ID NO: 2 in that it has one less isoleucine residue than the corresponding portion of SEQ ID NO: 2, and SEQ ID NO: 7 differs from SEQ ID NO: 2 in that it has a glycine at position 121 while SEQ ID NO: 2 has a glutamic acid at the corresponding position.

Claim 35 is drawn to an isolated gene encoding a protein having activity to synthesize aurones using chalcones as substrates, wherein said protein has the amino acid sequence of SEQ ID NO: 2. Claim 35 recites an isolated "gene" which encompasses genomic DNAs that include untranslated regions such as promoters and introns and 3' regulatory regions.

Claims 1 and 18 are so broad as to encompass nucleic acids encoding any possible enzyme that has the recited activity, provided the enzyme was isolated from a plant within the family Scrophulariales. This family has within it 95 different genera, most of which have multiple species within them. For example, the genus Agalinis has 42 species within it. The claims provide no structure to define the claimed nucleic acid. Neither the specification nor the claims provide any description as to what characteristics of a polypeptide would identify it or classify it as being "obtained" from within this genus of plants. That is, of all of the possible enzymes that have activity to synthesize aurones using chalcones, the specification does not provide any description as to how to identify the ones that are obtained from Scrophulariales.

Claim 27 is so broad as to encompass nucleic acids encoding any possible enzyme that has the recited activity, provided the enzyme was isolated from Antirrhinum majus. The claim

provides no structure to define the claimed nucleic acid. Neither the specification nor the claims provide any description as to what characteristics of a polypeptide would identify it or classify it as being "obtained" from within this plant species. That is, of all of the possible enzymes that have activity to synthesize aurones using chalcones, the specification does not provide any description as to how to identify the ones that are obtained from Antirrhinum majus.

Claims 5, 22, 38, 40, and 42 all recite that the claimed gene or nucleic acid encode a polypeptide that has a particular percent identity to instant SEQ ID NO: 2. However, the specification has not described where or how instant SEQ ID NO: 2 can be modified yet still retain the functionality required by the instant claims. Claims 39, 31, and 43 depend from 38, 40, and 42 and require that particular nucleic acid fragments be present in the encoded polypeptide sequence. These short fragments were sequenced during the discovery of the full length SEQ ID NO: 2, but there is no indication that they are necessary or sufficient to meet the functional limitations of the claims. Thus, even though these limitations provide some minimal structure for the claimed nucleic acid, that structure does not appear to be correlative or predictive of function, and still, the claim does not provide adequate written description for the claimed invention.

Likewise, claim 37 depends directly from claim 27 and claim 27, while providing a minimal structure for the claimed nucleic acids, does not provide adequate written description for the claimed nucleic acids. As noted, there is no indication that these fragments are are necessary or sufficient to meet the functional limitations of the claims. Thus, even though these limitations provide some minimal structure for the claimed nucleic acid, that structure does not appear to be

correlative or predictive of function, and still, the claim does not provide adequate written description for the claimed invention.

With regard to the claims which expressly claim genes and nucleic acids which encode SEQ ID NO: 6 or SEQ ID NO: 7, the specification provides only partial sequences in both of these cases. That is, the specification does not provide a full length coding sequence which encodes SEQ ID NO: 7 or SEQ ID NO: 6 as it is recited in the sequence listing, yet the claims clearly encompass these sequences, which are not described.

Of all of the potential nucleic acid sequences encompassed by the rejected claims, only a single example is provided in the specification, that is, the nucleic acid encoding SEQ ID NO: 2. Thus, applicant is in possession of nucleic acids encoding only a single amino acid sequence, that is SEQ ID NO: 2. Claims 1 and 35 are also drawn to genes, and encompass, therefore, genomic coding sequences. Such a sequence includes 5' and 3' untranslated regions, introns, and other regulatory sequences. However, applicant has only described the coding portion of the nucleic acid encoding SEQ ID NO: 2.

As noted in the scope of enablement rejection, the specification does not teach a nucleic acid that has the ability to synthesize any aurone except aureusidin. With regard to the functional requirement of the claims, applicant is in possession only of nucleic acids encoding SEQ ID NO: 2 which has the activity to synthesize aureusidin from chalcones.

Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities.

With regard to the written description, all of these claims encompass nucleic acid sequences different from those disclosed in the specific SEQ ID No:s which, for claims 5, 22, 38,

40, and 42 include modifications by permitted by the % identity language for which no written description is provided in the specification.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only nucleic acids encoding instant SEQ ID NO: 2 are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids that encode proteins modified by addition, insertion, deletion, substitution or inversion with respect to the disclosed SEQ ID No: 2 such that a different amino acid sequence is encoded which has the activity to synthesize aureusidin (or any other aurone) from chalcones.

Response to Remarks

The previously set forth rejections for new matter and under 112 2nd paragraph are withdrawn in view of the amended and cancelled claims. New 112 2nd and new matter rejections are set forth to address the pending claims.

112 1st, Scope of enablement

Applicant argues that using the guidance provided in the specification one skilled in the art could readily obtain other sequences which encode a protein having activity to synthesize aurones as instantly claimed. However, this does not address the fact that applicant has not taught one skilled in the art how to make and use the invention. Screening for molecules which may fall into the scope of the broad claims is not a teaching of how to make a particular nucleic acid. As previously noted, there is a high degree of unpredictability as to how instant SEQ ID NO: 2 can be modified yet still retain its function as being able to synthesize aureusidin, or can be modified so as to be able to synthesize a different aurone. The specification does not provide any guidance in this regard, indeed the specification only teaches a single molecule that has the ability to synthesize aureusidin from chalcones. A teaching of a general screening method cannot overcome the lack of additional guidance in light of the high level of unpredictability in the related technology.

Applicant argues that "a structural feature of the claimed nucleic acids is described (p. 10 of response)," yet this simply is not accurate for many of the rejected claims (for example claims 1, 6, 7, 8, 9, 18, 23, 24, 25, 26, 27, 28, and 29). Even for claims which recite some structure is provided, this structure is minimal allowing for a large number of amino acid changes relative to SEQ ID NO: 2 in the encoded polypeptide, while the specification does not provide any guidance as to how the sequence can be modified while retaining its enzymatic function.

Applicant argues that one skilled in the art would be able to practice the invention as claimed based upon the teachings of the specification using SEQ ID NO: 1 as a probe to obtain

other sequence which could encode a protein having activity to synthesize aurones as instantly claimed. However, this is not persuasive, because it is highly unpredictable, of all of the nucleic acids that would hybridize with instant SEQ ID NO: 1, which ones would have the ability to synthesize aurones by preferentially using chalcones as substrates. There is a complete lack of guidance in the specification as to how to select polynucleotides that encode enzymes having the ability to synthesize any aurone besides aurodesin. There is a compete lack of guidance as to how to select nucleic acids that encode enzymes that preferentially use chalcones as opposed to some other undefined substrate. The specification provides no guidance as to how SEQ ID NO: 2 can be modified while still arriving at a polypeptide with the recited activity. All of these are highly unpredictable areas, and absent further guidance the ordinary practitioner would not be able to practice the claimed invention commensurate in scope with the claims.

112 1st, Written description

Applicant asserts that the instant specification would describe the claimed genus to a person skilled in the art, presumably because the application describes how one skilled in the art could readily obtain additional genes and nucleotide sequences. However, this is not persuasive, because the issue is not COULD one obtain additional sequences, but instead, the issue is whether or not applicant had possession of the claimed invention at the time the invention was made or whether applicant adequately described the claimed invention to demonstrate such possession. In the instant application, the specification has demonstrated possession of a single cDNA nucleic acid molecule encoding a single polypeptide. Further, applicant argues that given the cDNA sequence one could obtain any full length genomic sequence. However, again, it is

noted that such sequences are not supported under written description. The court has stated, "While we have no doubt a person so motivated would be enabled by the specification to make it, this is beside the point for the question is not whether he would be so enabled but whether the specification discloses the compound to him, specifically, as something appellants actually invented. We think it does not." In Re Ruschig, 379 F.2d 990, 995, 154 U.S.P.Q. 118, 123 (CCPA 1967). Further, the court has stated "Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." The Regents of the University of California v. Eli Lilly & Co., 43 U.S.P.Q.2d 1406 (Federal Circuit 1997). In the instant case, it is not even clear that given the teachings of the specification one of skill in the art could in fact make the claimed invention. In either instance, the claimed invention does not meet the written description requirement for all of the reasons discussed herein.

Prior Art Rejections

The prior art rejections are withdrawn in view of the amendments to the claims which require that the nucleic acid sequences be "obtained" from particular plants.

Conclusion

9. Claims 31, 32, and 36 are allowed. The prior art does not teach or suggest an isolated nucleic acid encoding an amino acid sequence as shown in SEQ ID NO: 2, or an isolated nucleic acid sequence having the nucleotide sequence of SEQ ID NO: 1. Claims 33 and 34 would be allowable if they were amended to recite "An isolated host cell."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (703) 306-5824. The

examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM. Please note that on January 13, 2003 the examiner's telephone number will change to (571) 272-0753.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (703) 308-1119. Beginning January 13, 2003 Gary Benzion's telephone number will be (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196. Beginning January 13, 2003 the receptionist's telephone number will be (571)272-0507.

JEFFREY FREDMAN
PRIMARY EXAMINER

Juliet C Switzer
Examiner
Art Unit 1634

January 12, 2004